LEARNING FROM PRACTICE: SUBARACHNOID HEMORRHAGE – CAUSES AND CONSEQUENCES

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ABSTRACT

The authors present two cases of subarachnoid hemorrhage, both women, middle aged who developed almost the whole spectrum of complications of this type of intracranial bleeding. We briefly review the management of the subarachnoid hemorrhage and we emphasize the importance of the interventional therapy (treatment of the aneurysm by endovascular coiling or intraarterial catheterization and administration of Nimodipine for vasospasm) for the good prognosis of the patients.

Key words: aneurysm, subarachnoid hemorrhage, vasospasm, endovascular coiling

Abbreviations: SAH = subarachnoid hemorrhage, MCA = middle cerebral artery, ICA = internal carotid artery, ACA = anterior cerebral artery

Most frecquently the underlying cause of a SAH is a ruptured aneurysm (85%), 10% are caused by non-aneurysmal perimesencephalic hemorrhage and 5% by rare causes like arterial dissection (especially the vertebral artery in V4 segment), mycotic aneurysms, Ehlers-Danlos disease type IV, cerebral amiloid angiopathy, tumors, trauma, cerebral metastases from cardiac myxoma, meningeal carcinomatosis, radiation therapy, cocaine abuse a.s.o. The cerebral arteriovenous malformation usually do not rupture in the subarachnoid space; the vast majority form an intracerebral hematoma with or without extension into the subarachnoid space. Sometimes the arteriovenous malformation is located in the spine, and may be one of the causes for a SAH with a normal cerebral angiography.

Contrary to the common opinion, aneurysms are not congenital but develop during the course of life, usually after the second decade (1). The presence of anurysm in children is very rare and there is often an underlying cause, like trauma, infection or connective tissue disorders. In adults the estimated prevalence of aneurysms is 2,3%, the proportion tending to increase with age. They are located at sites of arterial branching, either in the circle of Willis or in the nearby branching point.

The exact reason for aneurysm developing is not known, but there are a number of factors which are incriminated, which can be divided in fundamental and clinical research:

- Genetic studies/ changes in structure of the wall
  - genes related to collagen type II-A1 and type I-A2 fibers, alfa 1 antitrypsine and SERPIN A3, related to serine proteinase inhibitors are only some of the genes involved
  - structural abnormalities determined by a disbalance between proteases and protease inhibitors, with a decrease of matrix metalloproteinases in the vessel wall is

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noticed not only in the wall of the aneurysm, but also in other extracranial and intracranial vessels as well as in skin biopsies.

- Clinical observations
  - Familial intracranial aneurysms are found in 10% of people with SAH
  - Autosomal dominant polycystic kidney disease or Ehlers Danlos type IV collagen disease are frequently associated with SAH, but both are very rare diseases so they cannot explain the majority of aneurysm developing cases
  - Common risk factors like smoking, arterial hypertension and excesive alcohol intake can be related both to aneurysms developing and rupture
  - People who suffered a SAH, are at risk to develop a new aneurysm (16% of the survivors develop a new aneurysm in the next 10 years)

Case 1: a 53 year-old-woman was hospitalized for left hemiparesis. She was previously known with arterial hypertension (not constantly treated) and obesity. The symptoms installed suddenly after a conflictual situation.

In the ER: somnolent, she answered with difficulty but correctly to simple questions, left hemiparesis without left hypoesthesia, she complained of intense occipital headache, and had nuchal rigidity; BP: 160/120 mm Hg; CGS score: 9 (O2V1M6).

The cerebral CT scan performed at the admittance showed the presence of blood in all the basal cisterns, in the interemispheric fissure and in the basal part of the sylvian fissure on the right side with compression on the temporal lobe (fig. 1, fig. 2).

The clinical aspect was strongly suggestive for a subarachnoid hemorrhage, combining headache with neurological deficit and nuchal rigidity; the clinical spectrum of aneurysmal subarachnoid hemorrhage can vary from sudden death to mild headache, so that approximately 15% die suddenly before reaching hospital and a part of the patients (<10%), either do not consult a physician or are not properly diagnosed by the primary care physician or even by the emergency physician (2).

CT scan is the first-line investigation if SAH is suspected because of the characteristic and rapid appearance of the extravasated blood.

Although it is not infaillible, the localisation of the blood can be an important guide in determining the presence and the site of the ruptured aneurysm, whether the hematoma is truly parenchimal or only distends the subarachnoid space.

The prediction of the site is correct in at least 90% of haematomas (3, 4). The presence of the blood in the frontal lobe, paramedially, on one or both sides, in the corpus callosum, the cavum septum pellucidi or between the frontal horns is indicating an aneurysm of the anterior communicating artery. The presence of blood in the lateral sylvian fissure with extension from this point mostly posteriorly and superiorly is suggestive for an aneurysm of the MCA. Rarely, the blood can extent medially, raising the problem of a differential diagnosis with the „hypertensive" hemorrhage, the distinction being made based on the lateral extension to the inner table of the skull in the case of an aneurysm. Aneurysms from the posterior circulation usually do not extent in the parenchyma.

The presence of blood in the medial part of the temporal lobe is indicating an aneurysm arising from the ICA, which are most often at the origin of the posterior communicating artery. The CT scan of our patient, with the blood accumulating around the temporal lobe was suggestive for this location.

Figure 1. *Blood accumulation and compression of the temporal lobe*

Figure 2. *Blood accumulation in the basal cisterns and in the right sylvian fissure*

For identifying the aneurysm we performed a catheter angiography. Some authors consider computed tomographic angiography (CTA) a reliable method for diagnosing the aneurysms, with a sensitivity up to 97% (5), although it is true that small aneurysms of 2-3 mm may escape detection with CTA (6). It has the disadvantage of injecting contrast material, but it can be performed immediately after the plain CT scan, while the patient is still in the machine.

Case 1: The angiography was performed practically in the first two hours from the admittance, and confirmed the presence of an aneurysm on the right ICA, situated nearly the origin of the posterior communicating artery (fig. 3, a and b).

The angiography is not a harmless procedure (7, 8), the main problems being the risk of transient or permanent neurological deficits (up to 1.8%) or the risk of aneurysm re-rupture (1-2% overall and 5% in the first 6 hours). In any event, if a surgical or endovascular intervention is in view, the angiography should be performed at the earliest opportunity, within 3 days of the initial bleed.

The treatment options for a ruptured aneurysm are either neurosurgical clipping, or endovascular coiling. The choice is based on the experience of centers for one method or the other, on the location and size of the aneurysm and on the status of the patient.

The purpose of both methods is to prevent re-bleeding (early or delayed), but neither of them offers 100% certainty. After rebleeding 80% of the

a)

b)

Figure 3. *(a) Digital substraction angiography: aneurysm located on the right ICA near the origin of the posterior communicating artery (black arrow); (b) 3D rotational substraction of the same image; the aneurysm is marked by the white arrow*

patients die or remain disabled, while after the initial bleeding the fatality rate is around 50% (still very high despite progresses in management of SAH). In the first hours after the initial hemorrhage 15% of the patients experience a sudden deterioration that suggests rebleeding. There is no reliable method to predict rebleeding. In patients who survive the first day, the risk is more or less evenly distributed over the next 4 weeks, being estimated at 40% for

the first 3 weeks (9), and without interventional procedures (surgical or endovascular) it remains at a constant level of about 3%/year.

Endovascular coiling (with platinum covered coils) tends to be today the first choice of treatment, at least in the centers with expertise, since it is perceived as being less aggressive and it has proven its efficacy both in the anterior, and posterior circulation. A systematic review of three randomized trials of coiling vs clipping, amongst which was the ISAT trial (2,143 patients), showed a relative risk of poor outcome in coiling of 0.76 (95% CI 0.67-0.88) and an absolute risk reduction of poor outcome of 7% (10, 11).

There are some things one has to keep in mind about endovascular occlusion:

- Location: aneurysms in the posterior circulation are usually more prone to coiling, whereas surgical treatment is often very difficult; aneurysms at the trifurcation of the middle cerebral artery are often difficult to coil without interfering major arterial branches
- Age: the risk of complications in patients > 70 years old are much higher for operation than for coiling
- The risk of rebleeding is slightly higher in coiling vs. clipping (2,6% vs. 1%) but the overall outcome (avoidance of death and dependence) still favors coiling.

The optimal timing is not established but taking into account the risk of rebleeding, "the sooner, the better"; if the procedure cannot be performed in the first 3 days there is no need to avoid the period between 4-12 days, considered unfavorable in surgery, since delayed cerebral ischemia is unlikely to be precipitated by endovascular occlusion.

The possible complications of coiling include (12): thromboembolism (4.7 %), re-bleeding during coiling (1.2%), herniation of a coil into the parent vessel, which may lead to ischemic damage, secondary infection of the thrombosed aneurysm, intracranial artery dissection. Some interventional radiologists start heparin during the interventional procedure to prevent thromboembolism and even advise 3 months of antiplatelet therapy, but this is not supported by randomized trials. When the herniation of the coil occurs this may need a surgical approach to retrieve the fragment. The aspect is illustrated in fig. 4, and occured in another case from our department, but fortunately did not complicate further with an ischemic lesion.

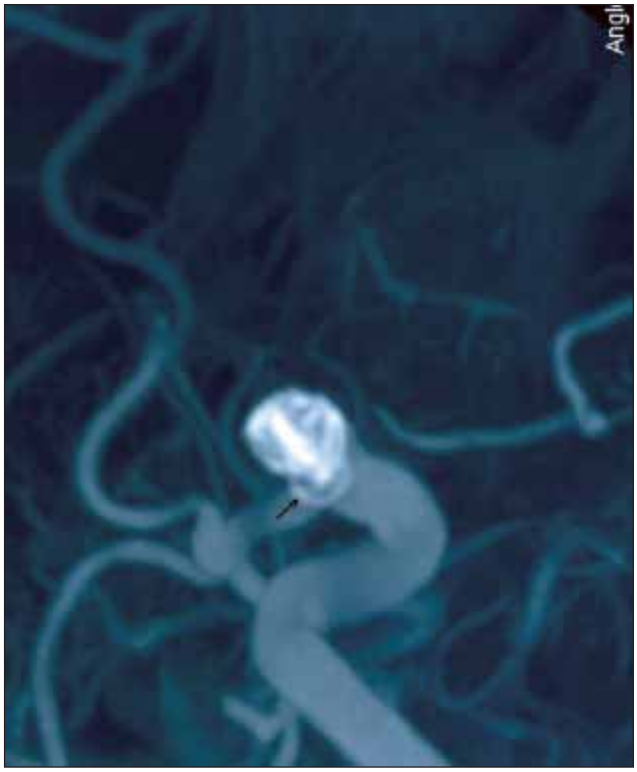
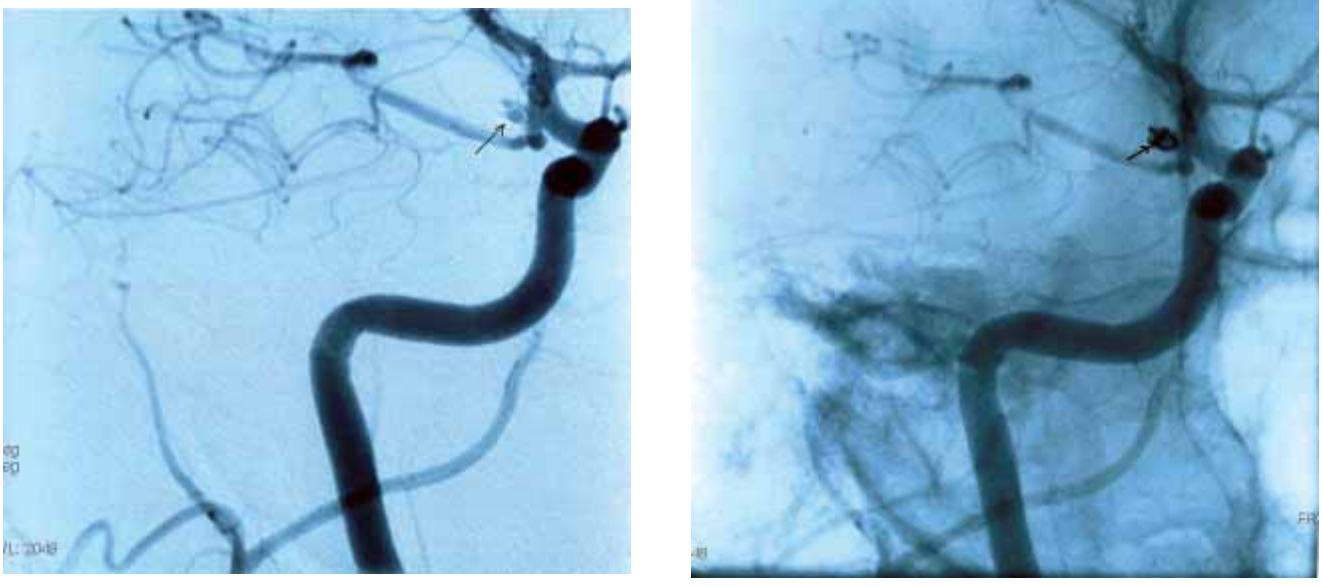


Figure 4. *Aneurysm of the ICA, filled with detachable coils; one coil has herniated in the main vessel (black arrow); this complication is most probably due to the large neck of the aneurysm (surgery would have been perhaps a better choice in this case)*

Case 1: An endovascular intervention was planned in the next 48 hours and was performed succesfully (fig. 5 a and b). The patient did not receive heparin during the procedure, or antiplatelet drugs after it. She received from day 1, oral Nimodipine, 180 mg/day

Follow up of the patients is still not standardized. Patients should be followed up with imaging within six months but if catheter angiography or magnetic resonance angiography are the best choice it is not proven yet. In the case of recanalization of the aneurysm's neck, currently most teams recommend re-coiling (13).

Surgical approach has now become the second choice although it has it's own advantages. The risk of poor outcome is 10% and the relative risk reduction is of 0.81 for surgical occlusion vs. no occlusion (14). The recommendation is to clip the aneurysms early, in the first 3 days, if possible in the first 24 hours, and this is no longer restricted to the patients admitted in good condition (15). Beside the prevention of rebleeding, some authors consider that early operation can also prevent development of delayed cerebral ischemia, because by eliminating the clots around the vessel the vasospasm



a) b)

Figure 5 (a,b). *The aneurysm filled with detachable coils (black arrows)*

is avoided; also in the case of appearance of the ischemic damage, hypertensive and hypervolemic treatment can be given whithout danger of rebleeding.

Case 1: The presence of the motor deficit on the left side was indicating a parenchymal damage, most probably due to the accumulation of the blood in the sylvian fissure. After coiling she had a favorable outcome, but 4 days later (7 days from the initial bleeding) she aggravated her left hemiparesis and developed an alien hand syndrome on the left side. The cerebral CT scan (fig. 6) revealed an ischemic stroke in the right MCA territory, and a subdural hematoma in the right temporal and parietal region, of 0.6 cm, and presence of blood around the anterior part of the right temporal lobe. The transcranial Doppler ultrasound examination did not reveal vasospasm or other abnormalities of the vessels.

Classically, in the acute phase of SAH there are no neurological signs other than those of meningeal irritation. If focal signs are present one can presume they are due to the accumulation of blood, either in the subdural space, in the cerebral parenchyma, or in the brain fissures, but it can result from raised intracranial pressure, from direct compression on the brain by the aneurysm or very rare and difficult to prove by embolism from the aneurysm itself (16).

Delayed cerebral ischemia is one of the major complications of an aneurysmal SAH. It does not

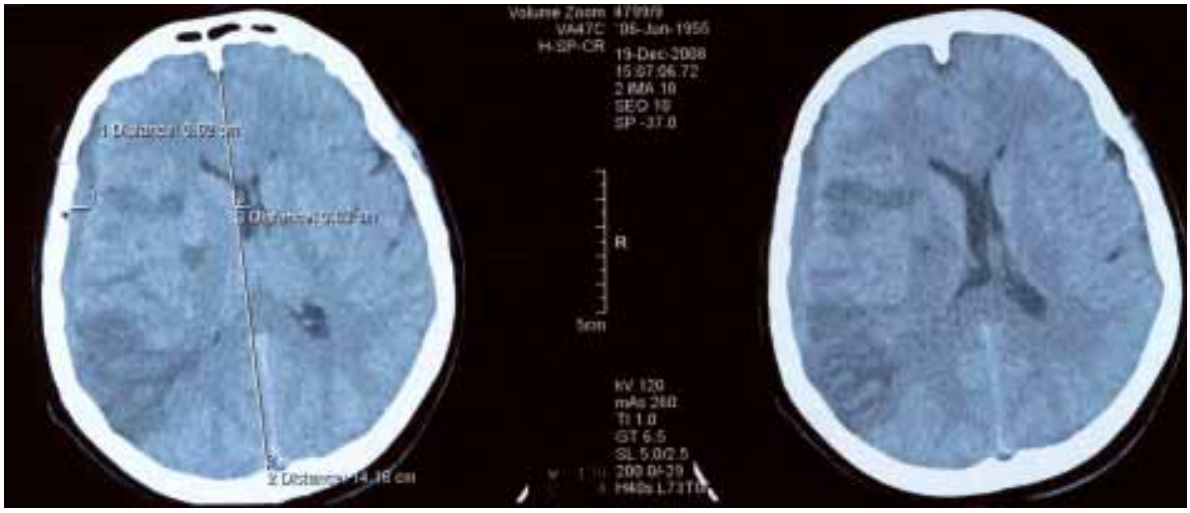


Figure 6. *Ischemic stroke in the right MCA territory and right subdural hematoma, with consecutive mass effect and midline shift towards left side.*

occur in non-aneurysmal perimesencephalic SAH. It can occur after a few days from the initial bleeding (between day 4 and 12), and it is strongly related to the amount of blood from the subarachnoid space (toxic substances released from clots, neuronal sensitization to hypoperfusion associated with raised intracranial pressure, arterial narrowing or hypovolemia). It is important to keep in mind that delayed cerebral ischemia is not synonymous with vasospasm (1/3 of the patients with ischemic stroke do not develop vasospasm and 1/3 of people with vasospasm do not develop brain ischemia) (17).

Delayed cerebral ischemia can determine focal neurological deficits, decrease in level of consciousness or both; a repeated cerebral CT scan will provide informations regarding the localization and extent of the ischemic area in almost 80% of the patients, but this will happen when the ischemic damage is already done. TCD monitoring for early diagnosis of vasospasm can be a solution for early diagnosing of the vasospasm but this will not be very helpful, since the predictive value of the vasospasm for cerebral ischemia is moderate. Nevertheless, if a "symptomatic" vasospasm is found, appropriate treatment can lead to improvement of the patient prognosis (see case no. 2). There are currently described two patterns: single cortical infarcts, typically near the ruptured aneurysm (like in our patient), and multiple widespread lesions, including subcortical locations and often unrelated to the site of aneurysm rupture (18).

The reason for developing ischemia in our case is not clear. Although the patient was monitored, it could have been a drop in the blood pressure, or it may be related to the surrounding blood in the sylvian fissure, even in the absence of vasospasm.

Prevention of delayed cerebral ischemia includes calcium antagonists (in a standard regimen of 60 mg, every 4 hours, 3 weeks) and maintainance of the plasma volume and hydroelectrolytic balance. Other drugs have been studied, like magnesium sulphate, with encouraging results, and even antiplatelet drugs or statins, but the number of patients was too small to draw sound conclusions.

The patient had received from the beginning, oral Nimodipine, 180 mg/day, the doses being adjusted according to BP monitoring. A Cochrane data base review (19) showed that nimodipine reduces the risk of poor outcome by about one third, but this results do not confirm in other calcium blockers and are largely based on a single randomized trial. The negative results of the trials using nimodipine via intravenous route are probably explained by the secondary hypotension. One should start with 30 mg every four hours (if tablets cannot be swallen they have to be crushed and administered on a nasogastric tube), under blood pressure monitoring, and then to increase the dose if the BP is stable.

When the delayed cerebral ischemia is installed there are two solutions: triple "H" regimen (haemodilutio-hypertension-hypervolemia) which is now controversial or transluminal angioplasty and vasodilating drugs administration (see case no. 2).

The risk of deliberately induced hypertension and hypervolemia include rebleeding, as well as the hemorrhagic transformation of the ischemic area, myocardial infarction or heart failure. In the last years the current opinion favors normovolemia instead of hypervolemia, considering there is a lack of evidence for hypervolemia (20). The main way to do it properly is to calculate 4 times a day the fluid balance in the first 10 days. Usually the quantity of fluids is 3 liters isotonic saline/day.

Maintaince of electrolyte balance is very important since both hyper-, or more frequent hyponatremia occur in SAH. Attributed incorrectly in the past to an inappropriate secretion of antidiuretic hormone, hyponatremia is the consequence of an excessive natriuresis ("cerebral salt wasting"). Predisposant factors are acute hydrocephalus (particulary the enlargement of the third ventricle) and ruptured aneurysm in the anterior communicating artery. Depending of the "cut-off" point, hyponatremia can occur in one third of the patients (sodium< 134 mmol/l) or in 2% (sodium < 125 mmol/l), and it develops most commonly betwen the second and tenth day (21). Our patient did not develop hyponatremia.

The subdural hematomas develop in 2-3% of all cases of aneurysmal rupture (22), more often after rebleeding than after a first episode. Usually they complicate the rupture of an aneurysm of the posterior communicating artery (like in our case). They are usually associated with blood in the subarachnoid space but can sometimes be the only manifestation of aneurysmal rupture. Blood passage to the subdural space implies a rupture of the arachnoid membrane and a possible explanation can be a previous adherence of the aneurysm to the arachnoid (usually as a result of a previous rupture, recognised or not). The management of this hematomas is not standardized; if they become life threatening, the immediate evacuation is mandatory, if not, they can resolve spontaneously.

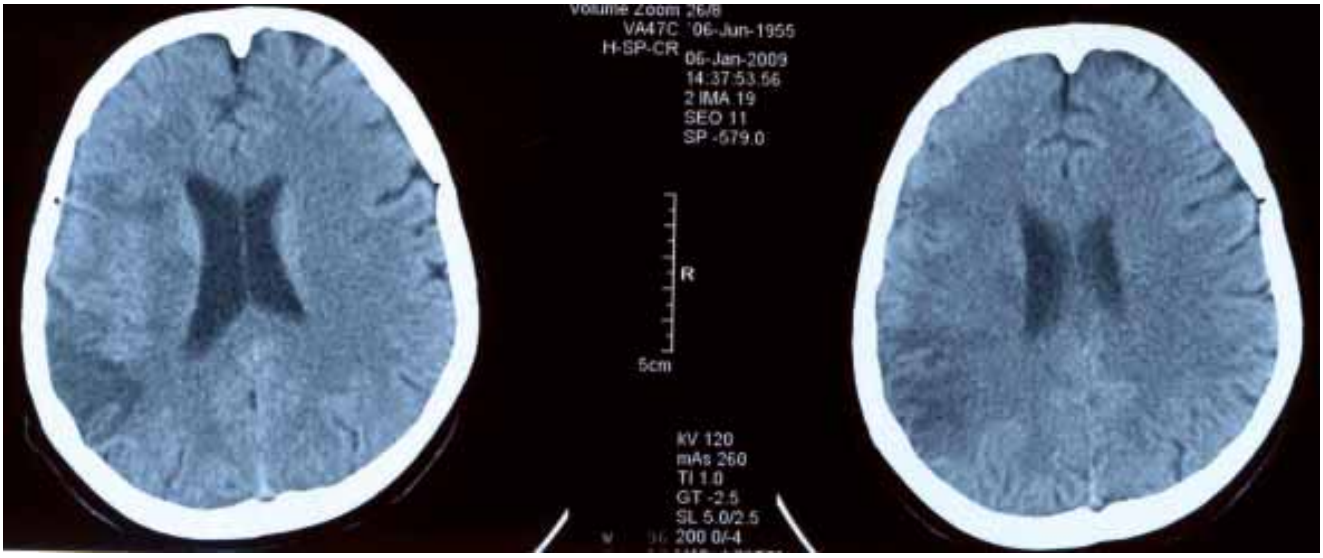


Figure 7. *Cerebral CT scan at 1 month from the initial bleeding showing resorbtion of the subdural hematoma*

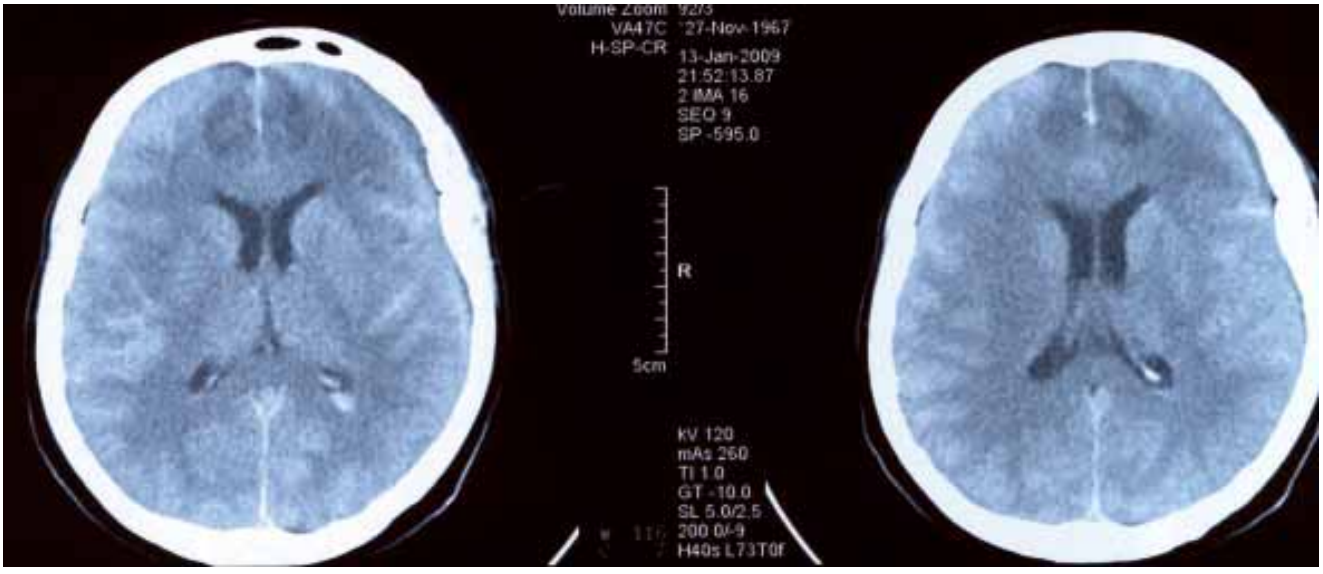


Figure 8. *Cerebral CT scan showing blood in the subarachnoid space and bilateral infarctus in ACA territory*

Case 1: The evolution of our patient was favorable. She recovered almost completely the motor deficit and the sensitive signs and symptoms. The CT scan done at 1 month from the initial bleeding, showed complete resolution of the blood, resorbtion of subdural hematoma and decrease in size of the ischemic hypodensity.

Case 2: A 40-year-old woman, previously hypertensive, not treated is aditted to the neurointensive care unit in state of coma, CGS = 3, suddenly installed while she was traveling in the city by tram. The initial CT scan showed blood in all subarachnoid spaces, with an accumulation in the anterior interemispheric fissure. After a few days she regained consciousness. She had tetraparesis. The angiography did not reveal any aneurysm. The evolution was slowly favorable, but 7 days after the initial bleeding she worsened her neurological status, developing cranial nerve paresis and aggravating the motor deficit. We repeated the CT scan which showed a bilateral frontal ischemia in the ACA territory (fig. 8). The Transcranial Doppler examination revealed high velocities of over 270 cm/sec, both in ACA and MCA territory, confirmed by angiography (fig. 9). We decided to administer Nimodipine by catheter angiography, and the procedure was performed in three consecutive days, under TCD monitoring. The vasospasm resolved (fig. 10) and the patient improved her neurological status. No aneurysm could be found in the second angiogram. The prognosis of this patients is poor due to the bilateral ACA infarctus, with persistent motor deficit and risk of developing dementia by strategic infarctus.

Figure 9. *Angiogram showing narrowing of the MCA and ACA (black arrow)*

Figure 10. *Normal caliber of the MCA and ACA after administration of Nimotop, by catheterization*

Only a few centers have reported on endovascular treatment of "symptomatic" vasospasm after SAH, the results being positive in more than half cases (23). We should be cautious because these data come from uncontrolled series and some of the studies reported only on arteries and not on patients. Endovascular treatment can consist of either transluminal angioplasty, or superselective catheterization and local administration of vasodilative drugs like papaverine or nimodipine. The results are inconclusive and the procedure is still regarded as an experimental procedure. In our patient the neurological status improved and the vasospasm resolved, and we consider the method deserves further researches.

In conclusion, although SAH is still a pathologic condition associated with high mortality and morbidity, we consider that close monitoring of the patients, preferable in a center with expertise (stroke unit or experienced center in cerebrovascular diseases), and interventional multidisciplinary approach, as soon as possible after the initial bleeding may considerably improve the prognosis of these patients.

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